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# OCULAR ASSOCIATIONS OF METABOLIC SYNDROME AT TERTIARY HEALTH CARE CENTRE -A CROSS SECTIONAL STUDY

Ophthalmology

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## ABSTRACT

**Introduction:** The increased prevalence of metabolic syndrome is becoming a significant public health challenge. Association of metabolic syndrome to age related cataract, glaucoma, macular degeneration and intraocular pressure has been emphasized in several studies. The present study was carried out to assess the ocular manifestations in metabolic syndrome. **Methodology:** The current study was the hospital based prospective cross-sectional study of Ocular associations of metabolic syndrome conducted among 20-80 years old patients. **Results:** Total 102 study subjects were enrolled in this study. The mean age of subject was 55.85 ± 11.08 years. Ocular manifestations exhibit a significantly higher mean age compared to those without ocular manifestations ($p < 0.001$). There was increased association of ocular manifestations amongst diabetic and Hypertensive patients. **Conclusion:** The findings of this study concluded that patients with age between 45 to 65 years were more at risk of developing ocular manifestation in metabolic syndrome. Cataract was the most common ocular manifestation followed by diabetic & hypertensive retinopathy. Where as Glaucoma & ARMD were diagnosed in equal prevalence followed by lid Xanthoma and central retinal vein occlusion.

## KEYWORDS

Metabolic syndrome, Ocular manifestation, Cataract, Diabetic retinopathy, Hypertensive retinopathy

## INTRODUCTION:

In 1920s, Kylin described metabolic syndrome as a cluster of conditions like hyperglycaemia, hypertension and gout.[1] Two decades later, adiposity was associated with metabolic conditions like cardiovascular diseases and diabetes.[2] Metabolic syndrome was once known as "Syndrome X" until its 1988 popularisation by Reaven.[3] When it comes to the specifics, the three most popular definitions put out by the WHO, the European Group for the Study of Insulin Resistance (EGIR), and the National Cholesterol Education Program—Third Adult Treatment Panel (NCEP ATP III) are very similar. However, you might find differences in the clinical criteria used to identify these components. They emphasize on four core components: dyslipidaemia, obesity, hypertension, and insulin resistance.[4] Pathogenesis of metabolic syndrome is complex and cannot be elucidated completely; however, two potential causative factors central obesity and insulin resistance appear to stand out. Altered cellular pathways associated with metabolic syndrome contributing to elevated oxidative stress and cellular senescence can lead to end organ damage.[5] Several other factors like genetics, pro-inflammatory state, ageing, hormonal dysregulation and inactive lifestyle can be associated with metabolic syndrome.[6]

In terms of public health, the increasing incidence of metabolic syndrome is a big concern.[7] Nearly a quarter of the world's population has metabolic syndrome, says the International Diabetes Federation.[8] Diabetes mellitus type 2, cardiovascular disease, and cerebrovascular disease are all known to be significantly increased by it.[8] It has been shown in multiple research that metabolic syndrome is associated with age-related cataract, glaucoma, macular degeneration, and intraocular pressure.[9]

Individual components of this syndrome have been long term linked with development of multiple eye diseases.[7] "The ocular diseases like diabetic retinopathy, glaucoma and cataract that are known to cause vision loss have been associated with diabetes and hypertension.[10] Retinopathy, cataracts, intraocular pressure, and dry eye illness are all linked to metabolic syndrome, according to research published in 2020 by Lima Fontes M et al.[10,11] Wu KY et al in 2022, found a positive link of association between ocular hypertension and central corneal thickness with metabolic syndrome in Olmsted country.[12] In their 2016 study, Poh et al. detailed the growing body of data connecting certain metabolic syndrome risk factors to ocular diseases, such as glaucoma and ARMD, respectively.[7] Chopra et al in 2012 found a link between metabolic syndrome and central retinal artery occlusion that potentially could lead to vision loss. However, the evidence of association was found to be weak. Inflammation of the small and larger vessels of eye and dysfunction of endothelium has also been positively linked with metabolic syndrome.[13]

No studies have been conducted in a tertiary care hospital environment to assess correlations between ocular symptoms and metabolic syndrome in Indian population. Finding the growing body of information linking metabolic syndrome to ocular disorders would aid in reducing the likelihood of developing these conditions and preventing damage that might result in irreversible vision loss. The study intends to ascertain whether the following conditions are associated with metabolic syndrome: oculomotor nerve palsy, cataracts, primary open angle glaucoma, hypertensive retinopathy, diabetic retinopathy, Lipemia retinalis, age-related maculopathy, central retinal artery occlusion, and central retinal vein occlusion.

### Methodology:

Participants in the trial were in the age group ranging from twenty to eighty attended at the KLES Dr. Prabhakar Kore Hospital and Medical Research Centre in Belagavi from August 2022 to July 2023. The hospital served as the site for the prospective cross-sectional study. The calculated sample size was 96 with assuming that, 50% have cataract among subjects with metabolic syndrome. The study subjects were enrolled in study by convenient sampling method who fulfilled inclusion criteria after obtaining the informed consent.

### Inclusion criteria:

Three out of the five components should be between the ages of 20 and 80 for this particular situation.

1. In this research, a big waist was defined as a man's or woman's waist circumference of more than 102 cm or 88 cm, respectively.
2. Hypertriglyceridemia is defined as blood triglyceride levels of 150 mg/dL (1.69 mM) or above.
3. For men, a low HDL cholesterol level is 40 mg/dL (1.04 mM) while for women, it is 50 mg/dL (1.29 mM).
4. Blood pressure is considered high when the diastolic measurement is 85 mm Hg or the systolic reading is 130 mm Hg.
5. A fasting glucose concentration of 110 mg/dL (6.1 mM) or above is considered high glucose.

**Exclusion Criteria:**

1. Patients with any other co-morbidities, other than obesity.
2. People with only obesity without any associated syndrome such as diabetes or hypertension or dyslipidaemia.
3. People with Congenital ocular deformities such as cloudiness of cornea, irregularly shaped pupil, opacities in the lens.

All study subjects age group above 20 years with metabolic syndrome interviewed with predesigned pre-tested questionnaire. Their details and thorough clinical history was obtained. All study participants underwent ocular examination to check for any anterior and posterior segment pathologies. Visual acuity was checked by using Snellen chart. Detailed fundoscopy with both Indirect Ophthalmoscope with 20 D Lens and Slit lamp Bio microscopy with 90 D Lens.

**Statistical Analysis:**

R version 4.3.2 statistical tools and Microsoft Excel were used for data analysis. Frequency tables that present categorical variables. Continuous variables presented in the form of Mean ± SD / Median (Min, Max). A chi-square test was used to examine if category variables are related. The QQ plot and the Shapiro-Wilk test are used to determine whether a variable is normal. Parametric tests are performed when the data has a normal distribution. Non-parametric tests are employed in the other case. To compare the mean of the variables across ocular manifestation, two sample t test or Welch's t test was applied. Mann Whitney test was used to compare the distribution of variables over ocular manifestation, utilize the U test. A P-value of 0.05 or less was regarded as statistically significant.

**RESULTS:**

Total 102 study subjects were enrolled in this study. Mean age was age 55.85 ± 11.08 years. About 61 (59.8%) were males and 41 (40.2%) were females. Abot 31 (30.39%) were farmers, 11 (10.78%) were retired and 29 (28.43%) were housewives. Occupations included in other categories like Pvt job, maid, guard, Gardner, student, painter, banker etc. (Table 1)

**Table 1: Socio-demographic parameter of study subject**

| PARAMETERS | | FREQUENCY | PERCENTAGES |
|---|---|---|---|
| Gender | Female | 41 | 40.2 |
| | Male | 61 | 59.8 |
| Occupation | Farmer | 31 | 30.39 |
| | Housewife | 29 | 28.43 |
| | Retired | 11 | 10.78 |
| | Shop Owner | 5 | 4.9 |
| | Teacher | 5 | 4.9 |
| | Daily wage worker | 4 | 3.92 |
| | Other | 18 | 17.64 |

**Table 2: Ocular examination of study subject**

| OCULAR EXAMINATION | | RIGHT EYE | LEFT EYE |
|---|---|---|---|
| Diminution of vision | No | 25 (24.51%) | 31 (30.39%) |
| | Yes | 77 (75.49%) | 71 (69.61%) |
| BCVA | <6/60 | 22 (21.57%) | 27 (26.47%) |
| | 6/60-6/36 | 25 (24.51%) | 25 (24.51%) |
| | 6/24-6/18 | 19 (18.63%) | 12 (11.76%) |
| | 6/12-6/6 | 36 (35.29%) | 38 (37.25%) |
| IOP (mmHg) | Mean ± S.D | 16.46 ± 4.91 | 15.74 ± 4.69 |
| | Median (Range) | 16 (7.8 - 34.2) | 15.6 (6 - 45) |

Out of 102 subjects, 77 (75.49%) had diminution of vision in their right eye while 71 (69.61%) had diminution of vision in their left eye. It was observed that 22 (21.57%) and 27 (26.47%) subjects had BCVA less than 6/60 in right eyes and left eyes respectively. Additionally, 25 (24.51%) in right eye and 25 (24.51%) in left eye had BCVA falling within the 6/60-6/36 range. The IOP of right eye ranged from 7.8 to 34.2 with mean IOP 16.46 ± 4.91 mmHg. The IOP of left eye ranged from 6 to 45 with mean IOP 15.74 ± 4.69 mmHg. (Table 2)

**Table 3: Distribution of different variables**

| VARIABLES | MEAN ± SD | MEDIAN (RANGE) |
|---|---|---|
| Waist Circumference (cm) | 102.38 ± 6.18 | 103 (89 - 115) |
| Serum Triglycerides (mg%) | 237.51 ± 60.76 | 234 (151 - 390) |
| HDL Cholesterol (mg%) | 34.96 ± 5.85 | 34.5 (19 - 48) |
| SBP (mm of Hg) | 156.71 ± 13.46 | 155 (138 - 190) |
| DBP (mm of Hg) | 88.02 ± 6.45 | 90 (70 - 110) |
| Fasting Blood Sugar (mg%) | 204.76 ± 61.9 | 187 (115 - 368) |

The waist circumference ranged from 89cm to 115 cm with mean of 102.38 ± 6.18 cm. The serum triglycerides ranged from 151 cm% to 390 mg% with mean of 237.51 ± 60.76 mg%. The HDL cholesterol ranged from 19 to 48 mg% with mean of 34.96 ± 5.85 mg%. The SBP ranged from 138 to 190 with mean of 156.71 ± 13.46 mmHg. The DBP ranged from 70 to 110 with mean of 88.02 ± 6.45 mmHg. The fasting blood sugar ranged from 115 to 368mg% with mean of 204.76 ± 61.9 mg%. (Table 3)

**Table 4 : Distribution of subjects according to different ocular manifestations.**

| OCULAR MANIFESTATIONS | SUB CATEGORY | NUMBER OF SUBJECTS (%) |
|---|---|---|
| Cataract | No | 9 (8.82%) |
| | Yes | 93 (91.18%) |
| Glaucoma | No | 90 (88.24%) |
| | Yes | 12 (11.76%) |
| Diabetic retinopathy | No | 75 (73.53%) |
| | Yes | 27 (26.47%) |
| HTN Retinopathy | No | 82 (80.39%) |
| | Yes | 20 (19.61%) |
| Central retinal vein occlusion | No | 98 (96.08%) |
| | Yes | 4 (3.92%) |
| Age related macular degeneration | No | 90 (88.24%) |
| | Yes | 12 (11.76%) |
| Lid Xanthoma | No | 97 (95.1%) |
| | Yes | 5 (4.9%) |

Among 102 subjects, 8 (7.84%) didn't have any ocular manifestations while 94 (92.16%) had one or the other ocular manifestations. About 93 (91.18%) had cataract, 12 (11.76%) had glaucoma, 27 (26.47%) had diabetic retinopathy, 20 (19.61%) had HTN retinopathy, 4 (3.92%) had central retinal vein occlusion, 12 (11.76%) had age related macular degeneration and 5 (4.9%) had lid Xanthoma. (Table 4)

From Welch's t-test, it is observed that the subjects with ocular manifestations exhibit a significantly higher mean age compared to those without ocular manifestations (p-value < 0.001). Additionally, the Mann-Whitney U test reveals that both systolic blood pressure (SBP) and diastolic blood pressure (DBP) are significantly elevated in subjects with ocular manifestations in comparison to those without. Furthermore, there was increased waist circumference, serum triglycerides, and fasting blood sugar levels among those with ocular manifestations. However, these differences did not reach statistical significance. HDL cholesterol levels were lower in individuals with ocular manifestations. However, this difference lacked statistical significance. (Table 5)

**Table 5: Comparison of different variables with ocular manifestation**

| VARIABLES | SUB CATEGORY | OCULAR MANIFESTATION | | P-VALUE |
|---|---|---|---|---|
| | | **No** | **Yes** | |
| Age (years) | Mean ± SD | 41.12 ± 4.05 | 57.11 ± 10.58 | < **0.001**$^{WT}$* |
| | Median (Range) | 41 (35 - 46) | 57 (29 - 80) | |
| Gender | Female | 4 (50%) | 37 (39.36%) | 0.7231$^{MC}$ |
| | Male | 4 (50%) | 57 (60.64%) | |
| Waist Circumference (cm) | Mean ± SD | 98.75 ± 7.89 | 102.69 ± 5.96 | 0.0833$^{t}$ |
| | Median (Range) | 97 (89 - 111) | 103 (89 - 115) | |

| | | | | |
|---|---|---|---|---|
| Serum Triglycerides (mg%) | Mean ± SD | 215.38 ± 36.85 | 239.39±62.14 | 0.4291[M W] |
| | Median (Range) | 206.5 (180 - 290) | 234 (151-390) | |
| HDL Cholesterol (mg%) | Mean ± SD | 38.75 ± 5.31 | 34.64 ± 5.8 | 0.0558[t] |
| | Median (Range) | 39 (30 - 47) | 34 (19 - 48) | |
| SBP (mm of Hg) | Mean ± SD | 148 ± 10.9 | 157.45 ± 13.44 | **0.0478[M W]*** |
| | Median (Range) | 143 (140 - 170) | 156 (138 - 190) | |
| DBP (mm of Hg) | Mean ± SD | 84 ± 4.66 | 88.36 ± 6.49 | **0.0304[M W]*** |
| | Median (Range) | 84 (78 - 90) | 90 (70 - 110) | |
| Fasting Blood Sugar (mg%) | Mean ± SD | 172 ± 46.16 | 207.55 ± 62.46 | 0.0730[M W] |
| | Median (Range) | 154 (136 - 256) | 187 (115-368) | |

**Abbreviation:** t – Two sample t test, WT – Welch's t test, MW – Mann Whitney U test, * indicates statistical significance.

## DISCUSSION:

Around the globe, metabolic syndrome is gaining significant attention as a major health concern. Its incidence has been rising steadily over the past few years. The International Diabetes Federation estimates that metabolic syndrome affects around 25% of the world's population. There is widespread agreement among definitions of metabolic syndrome that obesity, hypertension, dyslipidaemia, and hyperglycaemia are its main components. 11,265 people participated in a cross-sectional survey of the general public, which provided the data for this study. More US individuals with MetS than US patients without the syndrome experienced focal arteriolar constriction, lower retinal arteriolar diameters, larger retinal venular diameters, retinopathy, and arteriovenous nicking. These differences persisted even after accounting for variables like age, sex, race, education, alcohol consumption, and cigarette smoking.[14] It is commonly known that diabetes, hypertension, retinopathy, and other microvascular abnormalities are linked. Moreover, endothelial dysfunction in both big and small vessels, inflammation, and atherosclerosis affecting major arteries are linked to MetS. In 2012, the same or comparable findings were reported in a study of Japanese participants by Zhao et al. Retinal venule diameters were larger and artery diameters were smaller in these individuals, according to Saito et al.[15] Another Japanese investigation by Kawasaki et al. also found something similar. They found that the incidence of dry eye was almost twice as high in metabolic syndrome patients as in controls. [16]

Among the ocular symptoms seen in our research of individuals with metabolic syndrome, cataract was the most prevalent & significantly associated with older age. Cataracts and Met syndrome were linked in a study of middle-aged Europeans conducted by Paunksnis et al.[17] Met syndrome was linked to an increased likelihood of needing cataract extraction in a hospital-based research conducted in Italy.[18] Ocular manifestation was also not associated with gender in this study's univariate logistic regression analysis. Contrary to our findings, Harikrishnan et al.[19] found that elderly persons (OR=1.16) and women (OR=1.84) had a greater risk of ocular manifestation during univariate and multivariate logistic regression analysis in their research in Kerala. Bojarskiene et al. observed a statistically significant increased risk of cataracts in women with MetS.[20]

Diabetic retinopathy was the second most common ocular symptom, according to our research. Results from a 2016 study of Jewish individuals with type 2 diabetes showed that diabetic subjects with MetS had a significantly higher frequency of microvascular related difficulties than diabetic subjects without the syndrome.[21] The eye is only one of several organs that might be impacted by the systemic nature of diabetes mellitus. However, the onset and course of ocular problems in diabetes patients may be greatly affected by concurrent systemic illnesses. Retinopathy caused by diabetes may be prevented or slowed down with strict management of blood sugar and systemic hypertension.[22]

Among the eye conditions we examined, glaucoma ranked third in frequency. In a study conducted by Lee JS et al, results showed that people with metabolic syndrome had considerably greater intraocular pressure (IOP) than people without the condition.[23]

In our study samples, 11.76 percent of the participants had age-related macular degeneration. Numerous studies have found strong evidence connecting obesity to AMD. According to the age-related eye disease study (AREDS), researchers observed an increasing prevalence of age-related macular degeneration (ARMD) in fundus photographs as participants' BMI increased.[24] AMD is the most common cause of significant and irreversible vision loss in people living in industrialized countries.[25] Howard et al. found that early and late AMD were more common in nonsmoking women who were obese, defined as having a high body mass index or waist circumference.[26]

In our study, about 3.92% study subject had central retinal vein occlusion. The risk of RVO is increased by METS components, and the development of RVO is strongly impacted by raised blood pressure.[27]

Dyslipidaemia is often accompanied with xanthomas, which are common skin lesions that accumulate in certain areas, such as the buttocks, eyelids, trunk, extensor tendons of the wrists and elbows, Achilles tendon, and patellar tendon.[28] Patients with familial hyperlipidaemia type Ⅱa are more likely to develop significant hypercholesterolemia, which has been linked to these skin lesions. [29]

## CONCLUSION:

From this study we conclude that, most prevalent visual manifestation among the research individuals was cataract, followed by diabetic retinopathy and hypertensive retinopathy in that order. On the other hand, central retinal vein occlusion, lid xanthoma, age-related macular degeneration, and glaucoma were all detected in similar frequencies. Timely management of metabolic syndrome may prevent ocular manifestations. However, to confirm the casual relationship prospective interventional researches are required.

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